REMARKS

The Advisory Action mailed June 4, 2010 states that Applicant's Amendment filed May 24, 2010 has not been entered. Therefore, the above amendment is not inclusive of the amendment filed on May 24, 2010.

Claims 1-40, and 46-47 have been cancelled with this or a previous amendment.

Independent claims 54 and 55 have been amended to recite that the "wild-type" function of p53 has been restored. Support for this amendment can be found throughout the specification and specifically, for example, on page 7, lines 13-16.

Claims 41 and 48-51 have been amended to correct claim dependencies in light of the cancellation of claim 38. Claims 49 and 50 have been further amended to clarify the claim language so that is has proper antecedent basis as a result of the change in the claim dependencies.

Claims 56-63 are new. The support for new claims can be found in the claims as originally filed. *See, e.g.,* claims 11-21.

No new matter has been added by way of these amendments.

Claims 41-45, 48-51, and 54-63 are now pending.

Obviousness-Type Double Patenting Rejection

Claims 38, 41-45, 48-51, 54, and 55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 and 28-49 of co-pending Application Serial No. 10/493,582 ("the '582 application"). Claim 38 has been canceled, thus rendering the rejection moot as to this claim. Without acquiescing to the rejection and solely to expedite prosecution, the Applicant submits a terminal disclaimer herewith.

Accordingly, the Applicant respectfully requests reconsideration and withdrawal of the double patenting rejection.

Claim Objections

Claim 38 is objected to because of certain informalities. Applicant respectfully submits that claim 38 has been canceled, thus obviating this objection. Accordingly, Applicant respectfully requests withdrawal of the objection.

Rejections under 35 USC § 103

Claims 38, 41, 42, 45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al*. (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson"). Applicant respectfully disagrees with the rejection.

As the preliminary matter, Applicant respectfully submits that claim 38 has been canceled, thus rendering the rejection moot as to this claim.

It should be noted that many of the objections of record were directed to claim 38, which did not have all of the features of claims 54 and 55, the pending independent claims. Claims 54 and 55 are directed to a method of identifying a peptide of 2-8 amino acids in length having the ability to restore the wild-type function of p53 in an intra-cellular environment. The claimed method requires, *inter alia,* a step of screening a library (step a) and a step of identifying a peptide which is able to restore the wild-type function of p53 (step c). As previously explained, a library of peptides by definition refers to a collection of peptides of unknown sequence. The identity of the peptides which can restore wild-type function of p53 is only determined in step (c) of the method of claims 54

and 55. Applicant submits that such a method is not disclosed or suggested by the cited prior art alone or in combination.

The Shibata et al. reference describes methods of individually administering specific peptides of known sequence to host cells to determine whether they modify the activity of p53. In Shibata et al., specific cyclic peptides are synthesized as set out in Examples 1-14 (pages 24-30 of Shibata et al.) and these specific compounds of known sequence are then tested for their ability to restore the function of p53 (see e.g. Test Example 2, pages 18-19). Thus, unlike in the present invention, the amino acid sequences of Shibata peptides are known before they are administered to cells, so in contrast to the present invention, the Shibata et al. reference does not teach a method of identifying a peptide that can restore wild type p53 function from a library.

Moreover, Shibata et al. teaches that compounds capable of restoring p53 activity need to have the features recited in the abstract of Shibata et al., with preferred compounds being identified in Tables 1-1 and 1-2. The exemplified compounds are all cyclic peptides of at least 11 amino acids in length. Shibata et al. does not in any way suggest that much smaller peptides, namely peptides of 2 to 8 amino acids in length, could be useful in restoring the wild-type function of p53.

As previously explained, these deficiencies are not cured by the other references, none of which disclose or suggest that peptides of 2 to 8 amino acids in length could be useful in restoring the wild-type function of p53.

In the Advisory Action mailed June 4, 2010, the Examiner asserts that the Applicant has argued the references individually while the rejection is based upon a combination of the references. Applicant respectfully disagrees with the Examiner's conclusion. In order to expedite prosecution, however, Applicant has amended independent claims 54 and 55 to recite that the polypeptides restore the "wild type"

function of p53. Applicants submit that the cited references, in combination, do not teach or suggest the claimed method of identifying polypeptides that restore the "wild type" function of p53.

In the Advisory Action, the Office refers to the previous Office Action (mailed March 23, 2010) for an explanation of the motivation to combine the references. Specifically with regard to the combination of Daniels with Shibata and the other references, page 10 of the Office Action states that a person of ordinary skill in the art would have been motivated to use a library of peptides of small length, such as 3 to 6 amino acids, because Daniels teaches the need to identify small peptides that can interact with p53. In addition, the Office asserts that because Shibata, Daniel, and Tenson teach methods of using/screening peptide libraries having various lengths, it would have been obvious to one skilled in the art to substitute longer peptides (> 15 amino acids) for shorter peptides (3-6 amino acids) to achieve the predictable result of screening/using peptide libraries to identify peptides based on the purpose of the experimental design. Applicant respectfully disagrees. It is undisputed that Shibata does not teach peptides less than 11 amino acids in length that may be useful in restoring the wild-type function of mutant p53 (*see* page 8 of the Office Action mailed March 23, 2010), and that Shibata provides no reason to the one skilled in the art to use peptides of 2 to 8 amino acids in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring or modifying the function of p53. While Noaln teaches that screening assays could be used to identify peptides of varying length of 9 amino acids or greater that can "reactivate" or "compensate" for p53 activity, especially in tumor cells (*see, e.g.*, p. 37, ll. 25+; *see also*, p. 9 of the Office Action), Noaln does not address a method for identifying peptides of 2-8 amino acids in length.

Daniels does not cure the deficiencies of the combination of Shibata and Noaln. Daniels generally teaches the use of phage display libraries to identify peptides that bind to p53 (*see, e.g.*, Abstract). However, Daniels is silent on identifying peptides of 2-8 amino acids in length having the ability to ***restore the wild type function of mutant p53 in an intra-cellular environment***. The difference between the present invention and Daniels is significant and should not be ignored. The aim of Daniels was to "isolate phage that interacted with native human p53, to characterize the fine specificity of the interactions and make comparisons with known or unknown cellular partners of p53" (page 642, start of results section). Thus, Daniels discloses peptides which can recognize wild-type p53. Daniels teaches that peptides which recognize and bind wild-type conformation of p53 are much less likely to recognize a mutant conformation of p53 (see p. 645, column 2, last paragraph). Therefore, Daniels teaches away from the invention because Daniels suggests that one of skill in the art should not screen for polypeptides that bind to mutant p53. At the very least, Daniel suggests that the skilled artisan should not have a reasonable expectation of success in screening for polypeptides that restore the wild type function of mutant p53. Moreover, Applicants also disagree that the teachings of Tenson can be combined with the Shibata, Noaln and Daniels to establish obviousness of the pending claims. As discussed previously, Tenson generally discloses peptides that can confer erythromycin resistance. This is completely different field from the field of the present invention. While the Office Action asserts that Tenson motivates one of skill in the art to screen libraries in cells, the screening of cells for erythromycin resistance with a library of polypeptides is not related to screening for cells that have the wild type activity of p53 restored. It would in fact have been counter-intuitive for the skilled person to replace the peptides of Shibata, which Shibata discloses as being suitable for use in restoring p53 function, with the library of Tenson, which is disclosed for an entirely different purpose.

Since the combined disclosures of Shibata, Noaln, Daniels, and Tenson provide no reason for one skilled in the art to use peptides of 2 to 8 amino acids in length in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring the wild type of p53, the instant claims cannot be obvious over these references.

Finally, the Office asserts on page 10 of the Office Action that one skilled in the art would be motivated to use peptides of "various lengths" in the instantly claimed method because peptides of "various lengths" are disclosed in the art. First of all, the instant claims do not recite peptides of "various lengths"; instead, instant claims are directed to a method of identifying peptides of specific length, *i.e.,* 2-8 amino acids. Second, there is nothing in the cited art giving reason to the one skilled in the art to use peptides of 2 to 8 amino acids to restore the function of wild type mutant p53. As recently reiterated in *Bayer Schering Pharma AG v. Barr Laboratories Inc.*, 91 USPQ2d 1569, 1573 (Fed. Cir. 2009), generalities or vague or non-existent guidance towards the claimed invention is insufficient to render a claim obvious; there must be some reason for the ordinary artisan to make the *particular* invention being claimed. The cited art provides no reason for one of ordinary skill in the art to use peptides of 2 to 8 amino acids in a method of the instant claims.

More importantly, however, it has surprisingly been found that very small peptides can restore or modify the function of target proteins through interacting with target proteins *in vivo* and altering their conformation (see p. Specification p. 4, ll. 16-24). These results and findings are not predictable from the cited art and are an independent reason as to why the instant claims are non-obvious.

Accordingly, Applicants have sufficiently shown why the combination of Shibata, Noaln, Daniels and Tenson do not render obvious the claimed invention. Therefore,

Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 38, 41, 42, 45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al*. (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson"), and in further view of Thornborrow et al. (JBC Vol. 274(47): 33747-33756) ("Thornborrow").

Briefly, Thornborrow generally teaches p53-mediated transactivation of various promoters in different cells types. Applicants understand from the Office Action that the Examiner has applied Thornborrow against claim 42 specifically, and the Examiner has not alleged any teaching from Thornborrow against independent claims 54 and 55. As stated above. Indeed, the teachings of Thornborrow fail to cure the deficiencies of these references to render obvious independent claims 54 and 55. Accordingly, because claim 42 ultimately depends from claim 54, claim 42 Thornborrow in combination with the other cited references do not render the claims obvious for the reasons discussed above.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 38, 41-45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al*. (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson") and Thornborrow et al. (JBC Vol. 274(47): 33747-33756) ("Thornborrow"),

and in further view of Skarnes (US 5,767,336) ("Skarnes"). Applicant respectfully traverses this rejection.

Briefly, Skarnes generally teaches vectors and reporter gene products including a secretion signal peptide or a transmembrane domain. Applicants understand from the Office Action that the Examiner has applied Skarnes against claims 43 and 44 specifically, and the Examiner has not alleged any teaching from Skarnes against independent claims 54 and 55. Indeed, the teachings of Skarnes fail to cure the deficiencies of Shibata, Noaln, Daniels, Tenson, and Thornborrow to render obvious independent claims 54 and 55. Accordingly, because claims 43 and 44 ultimately depend from claim 54, Skarnes in combination with the other cited references do not render the claims obvious for the reasons discussed above.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

In the Advisory Action, the Office alleges that Takimoto et al. is considered pertinent to the Applicant's disclosure. The Applicant respectfully disagrees. Takimoto et al. is concerned with chemical compounds that can modify p53 function. By contrast, the method of the present invention allows the identification of peptides which can restore wild-type p53 function. The majority of commonly used drugs are based on chemical compounds and starting from Takimoto, the skilled person would have had no motivation to try to develop other types of drugs, such as peptide based drugs. He would not have tried identifying peptides that can modify the function of p53 with any reasonable expectation of success, particularly not peptides of 2-8 amino acids, because peptides are so different in their structure and function from chemical compounds such as those disclosed in Takimoto.

Thus, Takimoto does not cure the deficiencies of the other references.

Conclusion

The Applicant respectfully submits that in view of the foregoing arguments and amendments the claims are in condition for allowance, which the Applicant respectfully requests. If the Examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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